

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Patent Application of:	)	Group Art Unit: To Be Assigned
	)	
BECKER <i>et al.</i>	)	Examiner: To Be Assigned
	)	
Continuation Application of	)	Atty. Docket No. GP068-05.CN3
Application Serial No. 09/565,427	)	
	)	
Filed: March 14, 2001	)	
	)	
For: MODIFIED OLIGONUCLEOTIDES AND	)	
METHODS FOR DETERMINING THE	)	
PRESENCE OF A NUCLEIC ACID	)	
ANALYTE IN A SAMPLE	)	

**PRELIMINARY AMENDMENT**

Box Patent Application  
Commissioner for Patents  
Washington, D.C. 20231

Sir:

In connection with the above-captioned application, kindly enter the following preliminary amendments and consider the following remarks.

**Amendments**

**IN THE TITLE:**

Please amend the title of the invention to read --MODIFIED OLIGONUCLEOTIDES AND METHODS FOR DETERMINING THE PRESENCE OF A NUCLEIC ACID ANALYTE IN A SAMPLE--.

**IN THE SPECIFICATION:**

Kindly amend the specification as follows:

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Please amend the first sentence of the specification to read --This application is a continuation of application Serial No. 09/565,427, filed May 5, 2000, now pending, the contents of which are hereby incorporated by reference herein, which is a continuation of application Serial No. 08/893,300, filed July 15, 1997, now U.S. Patent No. 6,130,038, which claims the benefit of U.S. Provisional Application No. 60/021,818, filed July 16, 1996.--

At page 10, line 14, replace "Figure 1" with --Figures 1A, 1B and 1C--.

**IN THE SEQUENCE LISTING:**

Please amend the Sequence Listing by replacing originally filed pages 73 and 74 with substitute pages 73 and 74 filed herewith.

**IN THE CLAIMS:**

Please cancel claims 1-421 without prejudice.

Kindly add the following new claims:

422. (New) An oligonucleotide for determining the presence a nucleic acid analyte in a sample comprising:

a first base region having at least one ribonucleotide modified to include a 2'-O-alkyl substitution to the ribofuranosyl moiety; and

a second base region, wherein the first and second base regions hybridize to each other under nucleic acid assay conditions to form a hybrid more stable than a hybrid formed between unmodified forms of the first and second base regions, and wherein the oligonucleotide forms a hybrid with the nucleic acid analyte but not with a non-targeted nucleic acid under nucleic acid assay conditions, such that the nucleic acid analyte can be detected.

423. (New) The oligonucleotide of claim 422, wherein the first base region includes a cluster of at least about 4 ribonucleotides modified to include a 2'-O-alkyl substitution to the ribofuranosyl moiety.

424. (New) The oligonucleotide of claim 422, wherein the first base region includes at least one nucleotide which is not a ribonucleotide modified to include a 2'-O-alkyl substitution to the ribofuranosyl moiety.

425. (New) The oligonucleotide of claim 422, wherein each nucleotide of the first base region is a ribonucleotide modified to include a 2'-O-alkyl substitution to the ribofuranosyl moiety.

426. (New) The oligonucleotide of claim 422, wherein each nucleotide of the oligonucleotide is a ribonucleotide modified to include a 2'-O-alkyl substitution to the ribofuranosyl moiety.

427. (New) The oligonucleotide of claim 422, wherein the oligonucleotide includes a conjugate molecule.

428. (New) The oligonucleotide of claim 423, wherein the oligonucleotide includes a conjugate molecule joined to the oligonucleotide at a site located within the cluster of the first base region.

429. (New) The oligonucleotide of claim 422, wherein the oligonucleotide is up to about 100 bases in length.

430. (New) The oligonucleotide of claim 422, wherein the oligonucleotide includes a reporter group.

431. (New) The oligonucleotide of claim 430, wherein the reporter group comprises a fluorescent molecule.

432. (New) The oligonucleotide of claim 422, wherein the nucleic acid analyte comprises RNA.

433. (New) The oligonucleotide of claim 432, wherein the nucleic acid analyte comprises ribosomal RNA.

434. (New) The oligonucleotide of claim 422, wherein the oligonucleotide is a hybridization assay probe which forms a detectable hybrid with the nucleic acid analyte.

435. (New) The oligonucleotide of claim 422, wherein the oligonucleotide is an amplification primer for use in an amplification procedure.

436. (New) The oligonucleotide of claim 435, wherein the amplification procedure is a polymerase chain reaction method of amplification.

437. (New) The oligonucleotide of claim 435, wherein the amplification procedure is a transcription-based method of amplification.

438. (New) The oligonucleotide of claim 422, wherein the oligonucleotide is a target capture oligonucleotide.

439. (New) The oligonucleotide of claim 438, wherein the target capture oligonucleotide is immobilized by a solid support.

440. (New) The oligonucleotide of claim 422, wherein the 2'-O-alkyl substitution to the ribofuranosyl moiety is a 2'-O-methyl substitution.

441. (New) A method for determining the presence of a nucleic acid analyte in a sample, the method comprising the steps of:

- a) providing to the sample an oligonucleotide comprising:
  - i) a first base region having at least one ribonucleotide modified to include a 2'-O-alkyl substitution to the ribofuranosyl moiety; and
  - ii) a second base region, wherein the first and second base regions hybridize to each other under nucleic acid assay conditions to form a hybrid more stable than a hybrid formed between unmodified forms of the first and second base regions, and wherein the oligonucleotide forms a hybrid with the nucleic acid analyte but not with a non-targeted nucleic acid in the sample under nucleic acid assay conditions, such that the nucleic acid analyte can be detected;
- b) incubating the sample under conditions such that the oligonucleotide hybridizes to the nucleic acid analyte, if present; and
- c) determining whether the oligonucleotide has hybridized to the nucleic acid analyte.

442. (New) The method of claim 441, wherein the first base region includes a cluster of at least about 4 ribonucleotides modified to include a 2'-O-alkyl substitution to the ribofuranosyl moiety.

443. (New) The method of claim 441, wherein the first base region includes at least one nucleotide which is not a ribonucleotide modified to include a 2'-O-alkyl substitution to the ribofuranosyl moiety.

444. (New) The method of claim 441, wherein each nucleotide of the first base region is a ribonucleotide modified to include a 2'-O-alkyl substitution to the ribofuranosyl moiety.

445. (New) The method of claim 441, wherein each nucleotide of the oligonucleotide is a ribonucleotide modified to include a 2'-O-alkyl substitution to the ribofuranosyl moiety.

446. (New) The method of claim 441, wherein the oligonucleotide includes a conjugate molecule.

447. (New) The method of claim 442, wherein the oligonucleotide includes a conjugate molecule joined to the oligonucleotide at a site located within the cluster of the first base region.

448. (New) The method of claim 441, wherein the oligonucleotide is up to about 100 bases in length.

449. (New) The method of claim 441, wherein the oligonucleotide includes a reporter group.

450. (New) The method of claim 449, wherein the reporter group comprises a fluorescent molecule.

451. (New) The oligonucleotide of claim 441, wherein the nucleic acid analyte comprises RNA.

452. (New) The oligonucleotide of claim 451, wherein the nucleic acid analyte comprises ribosomal RNA.

453. (New) The method of claim 441, wherein the oligonucleotide is a hybridization assay probe which forms a detectable hybrid with the nucleic acid analyte.

454. (New) The method of claim 441, wherein the oligonucleotide is an amplification primer used in an amplification procedure.

455. (New) The method of claim 454, wherein the amplification procedure is a polymerase chain reaction method of amplification.

456. (New) The method of claim 454, wherein the amplification procedure is a transcription-based method of amplification.

457. (New) The method of claim 441, wherein the oligonucleotide is a target capture oligonucleotide.

458. (New) The method of claim 457, wherein the target capture oligonucleotide is immobilized by a solid support.

459. (New) The method of claim 441 further comprising the step of quantifying the nucleic acid analyte determined to be present in the sample.

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460. (New) The method of claim 454 further comprising the step of quantifying the nucleic acid analyte determined to be present in the sample.

461. (New) The method of claim 441, wherein step c) is indicative of the presence or absence of an organism or one or more members of a group of organisms in the sample.

462. (New) The method of claim 441 further comprising the step of providing to the sample a nuclease inhibitor other than a polynucleotide modified to include a 2'-O-alkyl substitution to the ribofuranosyl moiety of a ribonucleotide.

463. (New) The method of claim 441, wherein the 2'-O-alkyl substitution to the ribofuranosyl moiety is a 2'-O-methyl substitution.

\* \* \* \* \*

**Remarks**

Claims 422-463 are presently pending in the subject application.

Claims 1-421 have been canceled herein without prejudice to the future prosecution of the subject matter of these claims in this or a future continuation application.

The title of the invention has been amended to more properly reflect the currently claimed subject matter.

The specification has been amended to set forth Applicants' benefit of earlier filing date under 35 U.S.C. § 120 and to indicate that Figure 1 is a collection of three figures (*i.e.*, Figures 1A, 1B and 1C). Applicants submit that no new matter is being introduced by these amendments.

Consistent with their amendment dated March 18, 1998 in parent application Serial No. 08/893,300, Applicants are amending the Sequence Listing to provide updated contact and

application data information, as of March 18, 1998. This updated information does not constitute new matter and is reflected in the only computer readable form of the Sequence Listing filed in application Serial No. 08/893,300. Support for these non-substantive amendments to the Sequence Listing can be found in the original filing papers for application Serial No. 08/893,300.

Claims 422-463 are newly added and are supported by the originally filed claims and the specification *passim*. No new matter is believed to be introduced by the addition of these claims.

### Conclusion

Applicants submit that the subject application is in condition for allowance and early Notice to that effect is respectfully requested.

Please charge the excess claims fee due under 37 C.F.R. § 1.16(c), and any other fees which may be due, to Deposit Account 07-0835.

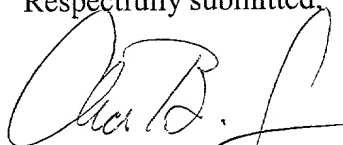
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Certification

I hereby certify that this correspondence (along with any referred to as being attached or enclosed) is being deposited on the date indicated below with the U.S. Postal Service as Express Mail No. EL612500464US addressed to Box Patent Application, Commissioner for Patents, Washington, D.C. 20231.

Respectfully submitted,



Date: March 14, 2001

By:

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